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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,450	04/27/2001	William H. Frey II	1871.01-US-U1	9084

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Jeffrey R. Stone
Altera Law Group, LLC
6500 City West Parkway, Suite 100
Minneapolis, MN 55344-7704

EXAMINER	
MCINTOSH III, TRAVISS C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 09/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/844,450	FREY ET AL.	
	Examiner	Art Unit	
	Traviss C. McIntosh	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-80* is/are pending in the application.

4a) Of the above claim(s) *2,3,5-31 and 45-80* is/are withdrawn from consideration.

5)☒ Claim(s) *4* is/are allowed.

6)☒ Claim(s) *1 and 32-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 13, 2005 has been entered.

The Amendment filed July 13, 2005 has been received, entered into the record, and carefully considered. The following information provided in the amendment affects the instant application by:

Claims 1, 4, 32, 34-35, 37, 41-42, and 44 have been amended.

Remarks drawn to rejections of Office Action mailed April 20, 2005 include:

112 1st paragraph rejections: which have been overcome in part by applicant's amendments and have been withdrawn in part.

112 2nd paragraph rejections: which have been overcome in part by applicant's amendments and have been withdrawn in part.

An action on the merits of claims 1, 4, and 32-44 is contained herein below. The text of those sections of Title 35, US Code which are not included in this action can be found in a prior Office action.

Claim Objections

Claim 32 is objected to because of the following informalities: the claim has been numbered two times (i.e., the claim reads "32. 32."). Appropriate correction is required.

Claim 44 is objected to because of the following informalities: claim 45 is listed at the end of claim 44 and does not start on a new line. Claim 45 should start on a new line. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The rejection of claims 1, 32-33 and 38-44 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of protecting the muscarinic acetylcholine receptor in Alzheimer's patients from inactivation caused by oxidative stress using the compounds of claim 1, optionally in combination with the compounds of claim 37, does not reasonably provide enablement for methods of protecting the muscarinic acetylcholine receptor in non-Alzheimer's patients from anything using compounds of claim 1, is maintained for reasons of record. Amended claims 34-36 are rejected for the same reasons. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Specifically, applicants are not enabled for methods of protecting a mAChR receptor from anything as in claim 1. Applicants are not enabled for the list of various disorders as set forth in claims 34-36. Applicants are not enabled for the use of the various enzymes, vectors, and proteins of claims 38-43.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in ***In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)***. A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

These factors include:
(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims - The nature of the invention

Claim 1 of the instant application is drawn to a method of protecting the mAChR receptor in Alzheimer's patients from anything comprising administering a pyrophosphate analog. Dependent claims 32-33 limit the compound to be used to various compounds such as pyrophosphate, imidodiphosphate, etc., Claims 34-36 provides that the subject suffers from various unrelated diseases such as cancer, heart disorders, irritable bowel syndrome, esophageal achalasia, and hereditary hematochromatosis, to name a few. Dependent claim 37 provides methods for combination therapy with various compounds. Dependent claims 38-43 provide for various combination therapies using vectors, enzymes, and proteins. Dependent claim 44 limits the compound to one that has 2-4 phosphorous molecules.

The state of the prior art

Antioxidants are known in the art to be chemical substances that neutralize the oxidant effects of free radicals and other substances. Compounds are known in the art to have varying degrees of antioxidant activity, as set forth by the differences of the 7-methoxychromones and 7-hydroxychromones (compound #556 and feruloyl aloesin) of Yu et al (US Patent 5,939,395). Antioxidants estrogen, vitamin E and vitamin C are known to have protected muscarinic acetylcholine receptors (mAChR) from inhibition by the low molecular weight inhibitor found in Alzheimer's disease patients or hemin (Venters et al., Brain Research, 764, pp. 93-100, 1997). The art is silent to the correlation between inhibition of mAChR in Alzheimer's patients and protecting any other tissue component from anything.

The level of predictability in the art

The examiner acknowledges the probability and predictability that the active agent of claim 1 has efficacy in Alzheimer's patients in protecting mAChR inactivation caused by oxidative stress, however the art is silent with regard to the predictability of the compound of claim 1 protecting the mAChR receptor from anything else. Additionally, the art is silent to the predictability of the combination therapy using the various agents of claims 38-43.

The amount of direction provided by the inventor

The instant specification is not seen to provide adequate guidance which would allow the skilled artisan to extrapolate from the disclosure and examples provided to use the claimed method commensurate in the scope with the instant claims. There is a lack of data and examples which adequately represent the scope of claim as written. The examiner notes, there has not been

provided sufficient instruction or sufficient methodological procedures to support the alleged efficacy instantly asserted using a compound from claim 1 and 4.

The existence of working examples

The working examples set forth in the instant specification are directed to the use of various compounds of claims 1 and 4 in testing for protection of mAChR from inactivation caused by the low molecular weight inhibitor found in Alzheimer's patients or heme/peroxide. It is noted that there has been no combination therapy tested. There were no tests or models for the use of the instantly claimed therapy in any other disease state. The results showed that various compounds do protect a mAChR from the inhibitory effects of the endogenous LMW inhibitor and heme/peroxide, thus allowing agonist/antagonist binding to the mAChR. However, there has not been provided sufficient evidence which would warrant the skilled artisan to accept the data and information provided in the working examples as correlative proof that the compound of claim 1 would indeed protect the mAChR receptor from anything, nor that patients being afflicted by the various diseases of claims 34-36 would be successfully treated using the instant therapy.

The quantity of experimentation needed to make and use the invention based on the content of the disclosure

Indeed, in view of the information set forth supra, the instant disclosure is not seen to be sufficient to enable the use of the compound of claim 1 in a method of protecting the mAChR receptor in Alzheimer's patients from anything without undue experimentation. One skilled in the art could not use the entire scope of the claimed invention without undue experimentation. One skilled in the art would be confronted with an undue burden of experimentation to isolate,

characterize, and test the various compounds of claim 1 to determine if indeed they have efficacy in protecting a mAChR receptor from any number of various things. One would be forced to also determine if the therapy of claim 1 would be acceptable in each of the various non-Alzheimer's disease states. One would also be required to formulate various compositions with the various proteins, vectors, enzymes, etc. of claims 38-43. As set forth supra, applicants have successfully shown methods of protecting the muscarinic acetylcholine receptor in Alzheimer's patients from inactivation caused by oxidative stress using the compounds of claim 1 and optionally with the other known antioxidants of claim 37.

Applicants stated that they believe the claims to be amended to overcome the rejection. However, it is noted that only claim 4 has been amended to overcome the enablement rejection set forth on the record.

Claims 33 and 37-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 33 is indefinite wherein the claim depends from withdrawn claim 31. It is noted that the examiner believes the claim to actually depend from claim 1.

Claims 37, 41, 42, and 44 all depend from claims "0 or 4". It is unclear how a claim can depend from claim 0. The examiner believes applicants intended the claim to depend from claims 1 or 4.

All claims which depend from an indefinite claim are also indefinite. ***Ex parte Cordova, 10 U.S.P.Q. 2d 1949, 1952 (P.T.O. Bd. App. 1989).***

Allowable Subject Matter

Claim 4 is allowed. The following is a statement of reasons for the indication of allowable subject matter: the prior art is not seen to teach or fairly suggest the use of the compounds of claim 4 in methods of protecting a mAChR receptor in an Alzheimer's subject from oxidative stress.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C. McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Traviss C. McIntosh III
September 16, 2005

James O. Wilson
Art Unit 1623
Supervisory Patent Examiner